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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/726,812	07/08/91	WEISS	S 028722-039

EXAMINER
ZISKA, S

ART UNIT	PAPER NUMBER
1804	13

18M2/0202
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1804

DATE MAILED: 02/02/94

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 11/9/93 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire three (3) month(s), ~~zero~~ (0) days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-93 are pending in the application.
   Of the above, claims 1-16, 19, 21-84 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 17, 18, 20, 85-93 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

This application should be reviewed for errors.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 17, 18, 20, remain under consideration; claims 85-93 have been newly added; claims 17, 18, 20 and 85-93 are examined in this Office Action.

35 U.S.C. 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 17, 18, 20 and 85-93 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 25-35 of copending application serial no. 07/961,813. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the claims embrace each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 17, 18, 20 and 85-93 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of copending application serial no. 07/967,622. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the claims embrace each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 17, 18, 20 and 85-93 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending application serial no. 08/010,829. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the claims embrace each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. *In re Vogel*, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d).

The newly presented grounds of rejection based on obviousness-type double patenting will not preclude the finality of this Office Action. Indeed, these grounds of rejections involve conflicting claims in copending applications newly discovered by the Examiner, all of which have two common inventors, the same assignee and the same attorney and applicants did not call the attention of the Office to any of the copending applications in the present application. It is noted that a total of 3 copending applications have been identified as being related to the present application and thus clearly material to the examination thereof. Further note that all 3 applications were filed well before the mailing of the first action on the merits. It is therefore apparent that Applicants had ample time in which to bring the other applications to the attention of the Office. Applicants will not be permitted to extend the prosecution of the present application by reasons

of their inaction with regard to notice to the Office of conflicting claims in copending applications, the discovery of which necessitated the new grounds of rejections at this advanced point in the prosecution. Indeed, with appropriate notice, these grounds of rejections clearly could have been incorporated in a prior Office Action. This situation is clearly analogous to the policy of making an action final where applicants' material amendments to the claims necessitated a new ground of rejection, since in both instances it is applicant who caused the rejection to be applied after the case had received an action on the merits. See MPEP Section 706.07(a).

The declaration submitted by inventor Reynolds is acknowledged, has been considered and is discussed below. The declaration overcomes some rejections, and fails to overcomes others, as explained below.

The rejection of claim 17 under 35 U.S.C. 112, first paragraph, is withdrawn for reasons set forth below. However, Applicants' amendments to claim 17 have necessitated new grounds of rejection and therefore this action will be made Final. Note that the original rejection regarding limiting the claims to brain and striatal tissue has been withdrawn in view of the amendment to the claim limiting the claim to neural tissue; that the original rejection regarding limiting the claims to mice has been withdrawn in view of evidence presented in the declaration; that the original rejection regarding limiting the claims to a EGF at a particular concentration is withdrawn; that the rejection regarding the limitation of the claim to the culture substrate actually used is withdrawn in view of the amendments to the claim and that the rejection regarding the method actually used by Applicants to isolate the cells from the mammal is withdrawn in view of the amendments to the claim. Regarding the submission of new pictures, the submission is acknowledged.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact

terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an adequate written description of the invention and for failing to teach how to make and/or use the invention as claimed, i.e. failing to provide an enabling disclosure. Applicants have disclosed proliferation of multipotent stem cells from fetal or embryonic neural tissue from humans and mice but have failed to provide evidence showing proliferation of neural tissue from adults or juveniles. Applicants have disclosed in the declaration that the intermediate filament, nestin, is found on undifferentiated neural tissue (declaration, page 6, top paragraph) but have failed to positively show for cells derived from adult tissues that undifferentiated cells have proliferated. Note that Applicants have tested for the expression of differentiated markers such as GFAP and NSE and have simply failed to test for the presence of nestin expression, stated in the declaration to be the marker for undifferentiated neural tissue. Lack of differentiation must be tested for just as presence of differentiation must be tested for and Applicants have failed to provide evidence that cells derived from adult tissue actually give rise to multipotent stem cells and therefore that the mammalian neural tissue contained at least one multipotent stem cell. Therefore, Applicants' arguments (page 20 this amendment) that they were the first to show that adult brain tissue can ggive rise to large number of multipotent stem cells is not persuasive. Regarding Applicants' further arguments that claim 92 is not rendered obvious by the prior art, note that the independent claim, claim 17, does not claim adult tissue and the combination of references renders obvious the claimed invention for reasons as set forth below.

Regarding claims 18 and 20, as stated above, Applicants have failed to provide evidence that adult tissues obtained from the adult mouse and human would give rise to multipotent stem cells and that the stem cells

could be proliferated in vitro since Applicants have failed to test for the undifferentiated state (nestin positive).

Regarding claim 85, Applicants have failed to disclose evidence that amphiregulin would have the claimed results, which is the proliferation of multipotent stem cells in vitro.

Regarding claim 88, Applicants have failed to provide evidence that the stem cells may be proliferated in vitro without limit and there is no evidence in the art that stem cells of any type may be proliferated without limit. If Applicants are aware of art teaching that stem cells may be proliferated in vitro without limit, the art should be submitted for consideration. Note that the phrase "without limit" may be interpreted as being immortalized and clearly the stem cells are not immortal.

Regarding claim 92, drawn to adult and juvenile sources of adult mammals, the issue has been addressed above in the rejection of claim 17.

Regarding claim 93, the issue of differentiation or lack thereof has been addressed in the rejection of claim 17.

Claims 17, 18, 20 and 85-93 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification.

Claim 93 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The word "substantially" is vague and unclear since the degree of differentiation lacks metes and bounds. Cells are either differentiated or they are not.

The rejection of claims 17, 18 and 20 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendments to the claims.

The rejection of claims 18 and 20 under 35 U.S.C. 112, first paragraph, limiting the claims to mouse brain and striatal tissue and mouse EGF at a concentration of 20 ng/ml is withdrawn.

Claim 87 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "preexposed to serum" is vague and unclear since when the preexposure takes place is not apparent. This terminology is confusing since it is not known in the art to expose cells to serum before putting the cells into a medium and that the culture medium usually contains serum.

The rejection of claim 17 under 35 U.S.C. 102(a) as being anticipated by Cattaneo is maintained. Applicants' arguments, filed November 9, 1993, have been considered but not found to be persuasive. Applicants have argued that Cattaneo does not disclose the proliferation of multipotent stem cells and that the cell described by Cattaneo appears to be a unipotent progenitor cell, capable of differentiation only into neurons. However, contrary to Applicants' arguments, the cell of Cattaneo is a multipotent stem cell since the cell was capable of at least two pathways, proliferation of the stem cell phenotype, or differentiation into neurons. Thus, since the cells of Cattaneo had at least two fates, the cells are considered to inherently be multipotent stem cells, lacking evidence to the contrary.

Applicants have further argued that Cattaneo fails to teach a method for achieving proliferation without limit. However, claim 17 does not claim proliferation without limit.

Applicants have argued that claims 88-93 are not anticipated by Cattaneo. However, claims 88-93 were not rejected over Cattaneo and therefore Applicants' arguments are moot.

The rejection of claim 17 under 35 U.S.C.102(b) as being anticipated by Morrison is withdrawn. Applicants' arguments are therefore not addressed.

The rejection of claims 18 and 20 under 35 U.S.C. 103 as being unpatentable over Cattaneo as applied to claim 17 above and further in view of Morrison is withdrawn in view of the amendments to the claims. Applicants' arguments which are directed to the application of Cattaneo and further in view of Morrison to newly added claims 85-93 are moot since claims 85-93 were not included in the original ground of rejection. Such arguments are therefore not addressed.

The rejection of claims 17, 18 and 20 under 35 U.S.C. 103 as being unpatentable over Weiss taken with Anchan or Morrison is withdrawn in view of the amendments to the claims and the amendments have necessitated a new ground of rejection, set forth below. Applicants' arguments are therefore not addressed.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> "A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."
>
> (f) he did not himself invent the subject matter sought to be patented."

Claims 17, 85-90 are rejected under 35 U.S.C. § 102 (a) as being anticipated by Anchan (Neuron). Anchan discloses that EGF and TGFalpha

stimulate proliferation of retinal neuroepithelial cells in primary cultures in vitro. Anchan discloses that the neuroepithelial cells generate a large variety of different neuronal cell types and therefore Anchan inherently discloses a multipotent stem cells. Therefore Anchan discloses exposing the multipotent stem cell to a culture medium containing at least one growth factor since Anchan discloses exposing the cells to EGF and TGFalpha.

Regarding claims 85 and 86, Anchan discloses exposing the cells to EGF.

Regarding claim 87, Anchan discloses culturing the cells in a defined culture medium using serum and does not disclose that the cells are pre-exposed to serum in vitro.

Regarding claim 88, stem cells are known to be capable of multiple divisions by definition and Anchan discloses that the stem cells used are multipotent progenitor cells.

Regarding claims 89 and 90, Anchan discloses proliferation of cells in a suspension culture and plating the cells onto a fixed substrate such as polylysine, laminin or Matrigel (page 934, column 2, first paragraph under Experimental Procedures).

Therefore the reference anticipates the claims.

Claims 17 and 89 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Temple. Temple discloses in vitro proliferation of blast cells isolated from embryonic rat forebrain, mechanical dissociation of the cells into a single cell suspension, exposing the cells to a culture medium containing at least one growth factor which caused the cells to proliferate (first paragraph). Note that Temple exposed the cells to culture medium conditioned by a primary bulk culture of cells and that conditioned medium is known in the art to add growth factors or soluble cellular products necessary for cell growth to the medium. Therefore Temple inherently

discloses exposing the cells to a culture medium containing at least one growth factor.

Regarding claim 89, Temple discloses a cellular suspension of cells and does not plate out the cells onto a substrate so Temple therefore inherently discloses a method wherein the cell is proliferated in suspension.

Therefore, the reference anticipates the claims.

Claims 17, 18, 85-88, 90 and 93 are rejected under 35 U.S.C. § 102 (a) or (b) as being anticipated by Reynolds, Tetzloff and Weiss (Abstract 474.2), hereafter known as Reynolds (474.2). The exact date of publication is not apparent. Reynolds discloses that EGF and TGFalpha cause proliferation of mouse neural (striatal) cells in in vitro culture. Reynolds further discloses that the dividing precursors formed proliferating clusters. Reynolds inherently discloses that the cells were dissociated since Reynolds discloses that 1250 cells/square cm were plated. It is not possible to count cells in a clump since clumps are three dimensional in nature and the scientist cannot see the other side of the clump to count the cells.

Regarding claim 18, Reynolds discloses use of mouse cells.

Regarding claims 85 and 86, Reynolds discloses use of EGF, a known growth factor.

Regarding claim 87, Reynolds discloses use of defined serum free medium. Reynolds fails to disclose that the cells were preexposed to serum; therefore Reynolds inherently discloses that preexposure of the cells did not occur.

Regarding claim 88, stem cells are by definition multipotent and the cells of Reynolds displayed multiple cellular fates.

Regarding claim 90, Reynolds discloses plating the cells to achieve differentiation.

Regarding claim 93, Reynolds inherently discloses that the multipotent stem cell proliferated 21 DIV with substantially no differentiation since Reynolds discloses that at 21 DIV, the cell cluster was still growing and therefore the stem cells necessarily had to be proliferating in order to give to greater and greater number of differentiated cells. Note that it is well known in the art that differentiated cells do not divide.

Therefore the reference anticipates the claims.

Claims 17, 18, 85-88, 90 and 93 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Applicants' publication (Abstract 474.2, in Journal of Neuroscience, volume 16, 1990) lists an inventor, Dr. Tetzloff, not listed on the instant application. Accordingly, an explanation in declaratory form of why Dr. Tetzloff is not listed as an inventor in the present application is required to overcome the rejection.

Claims 17, 18, 85, 86, 87, 88 and 90 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Applicants' publication (Journal of Neuroscience, volume 12(11), 1992) lists an inventor, Dr. Tetzloff, not listed on the instant application. Accordingly, an explanation in declaratory form of why Dr. Tetzloff is not listed as an inventor in the present application is required to overcome the rejection.

Claims 91 and 92 are rejected under 35 U.S.C. 103 as being unpatentable over Anchan (Neuron) as applied to claims 17, 85-90 above, and further in view of Reh et al. Claims 17 and 85-90 were rejected under 35 U.S.C. 102(a) for reasons as stated above. Reh discloses culturing isolated cells in vitro to the aggregate stage and then dissociating the cells to cause differentiation (page 4188, column 1, last paragraph). Reh further discloses

that the types of cells produced were those that were primarily being generated at the time of dissociation. Therefore, Reh discloses that the cells were differentiating in the clump or aggregate at the time of dissociation.

Regarding claim 92, it would have been obvious to one of ordinary skill to apply the techniques of Anchan to tissue from adult and juveniles in order to obtain proliferation of multipotent stem cells in view of the teachings of Anchan that in larval amphibians removal of the retina induces a dramatic regeneration of in the remaining marginal neuroepithelial cells (page 923, column 1, first paragraph).

Reh provides the motivation to combine the references since Reh discloses that different neuronal types arise at different times during neurogenesis and that the factors that determine cell type must be developmentally regulated as well. It would have been obvious to modify the method of Anchan by allowing the cells to differentiate in aggregates since Reh discloses that cells in aggregates are differentiating.

Accordingly, the modification of the method of Anchan by inducing the cells to differentiate in suspension as suggested by Reh in order to obtain a method for the in vitro proliferation of a multipotent stem cell was within the ordinary skill in the art at the time the claimed invention was made. From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 85-90 are rejected under 35 U.S.C. 103 as being unpatentable over Cattaneo as applied to claim 17 above, and further in view of Anchan (Neuron, volume 6, 1991). Claim 17 was rejected under 35 U.S.C. 102(a) for reasons as stated above. Regarding claims 85 and 86, Anchan discloses exposing the cells to EGF.

Regarding claim 87, Anchan discloses culturing the cells in a defined culture medium using serum and does not disclose that the cells are pre-exposed to serum in vitro.

Regarding claim 88, stem cells are known to be capable of multiple divisions by definition and Anchan discloses that the stem cells used are multipotent progenitor cells.

Regarding claims 89 and 90, Anchan discloses proliferation of cells in a suspension culture and plating the cells onto a fixed substrate such as polylysine, laminin or Matrigel (page 934, column 2, first paragraph under Experimental Procedures).

Cattaneo provides the motivation to combine the references on page 765, second column, wherein it is stated that other members of the NGF family might promote both the proliferation of neuronal precursors and the survival/differentiation of neurons derived from these precursors. Therefore, it would have been obvious to one of ordinary skill to substitute the EGF or TGFalpha for the NGF of Cattaneo in order to obtain in vitro proliferation or differentiation of neural stem cells.

Accordingly, the modification of the method of Cattaneo by using EGF to proliferate the stem cells as suggested by Anchan in order to obtain a method for the in vitro proliferation of a multipotent stem cell was within the ordinary skill in the art at the time the claimed invention was made. From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 17, 85, 86, 89 rejected under 35 U.S.C. § 102 (b) as being anticipates by Anchan et al (Abstract 308 in J. Cell. Biol., volume 109,

September, October 1989; Abstract 308, hereafter). Anchan discloses culturing germinal neuroepithelial cells of the rat retina in EGF and that such culturing increased the cellular proliferation. Anchan inherently discloses that the germinal epithelial cells were multipotent stem cells since the cells either proliferated or differentiated, thus demonstrating that the cells had multiple fates. Anchan inherently discloses that the tissue was dissociated since cell aggregates of 5 cells were obtained.

Therefore, the reference anticipates the claims.

Claims 18, 20, 87, 90-93 are rejected under 35 U.S.C. 103 as being unpatentable over Anchan (Abstract 308) as applied to claims 17, 85, 86, 88 and 89 above, and further in view of Anchan (Neuron volume 6, 1991) and Reh. Claims 17, 85, 86, 88 and 89 were rejected under 35 U.S.C. 102(b) for reasons as stated above.

Regarding claims 18 and 20, it would have been obvious to one of ordinary skill to apply the techniques of Anchan (Abstract) to the neural tissue of other species and have a reasonable expectation of success in obtaining proliferation of the stem cells since the neural tissue from other species would be expected to respond in a similar manner as the rat tissues to the particular species specific growth factors. Note that one of ordinary skill would known to use the appropriate specific growth factor and that in addition, one of ordinary skill would be able to determine by routine experimentation which growth factors exhibit cross reactivity in other species.

Regarding claim 87, Anchan discloses culturing the cells in a defined culture medium using serum and does not disclose that the cells are pre-exposed to serum in vitro.

Regarding claim 90, Anchan discloses proliferation of cells in a suspension culture and plating the cells onto a fixed substrate such as

polylysine, laminin or Matrigel (page 934, column 2, first paragraph under Experimental Procedures).

Regarding claim 91, Reh discloses culturing isolated cells in vitro to the aggregate stage and then dissociating the cells to cause differentiation (page 4188, column 1, last paragraph). Reh further discloses that the types of cells produced were those that were primarily being generated at the time of dissociation. Therefore, Reh discloses that the cells were differentiating in the clump or aggregate at the time of dissociation.

Regarding claim 92, it would have been obvious to one of ordinary skill to apply the techniques of Anchan to tissue from adult and juveniles in order to obtain proliferation of multipotent stem cells in view of the teachings of Anchan that removal of the retina or toxic damage induces a dramatic regeneration of in the remaining marginal neuroepithelial cells (page 923, column 1, first paragraph).

Regarding claim 93, it would have been obvious to one of ordinary skill to culture the cells as long as possible in order to determine the length of time that stem cells are produced since Anchan (Abstract 308) is clearly interested in the elucidating the factors involving stem cell proliferation.

Reh provides the motivation to combine the references since Reh discloses that different neuronal types arise at different times during neurogenesis and that the factors that determine cell type must be developmentally regulated as well. It would have been obvious to modify the method of Anchan by allowing the cells to differentiate in aggregates since Reh discloses that cells in aggregates are differentiating.

Accordingly, the modification of the method of Anchan (Abstract 308) by inducing the cells to proliferate in vitro as suggested by Anchan (Neuron) and Reh in order to obtain a method for the in vitro proliferation of a multipotent stem cell was within the ordinary skill in the art at the time the

claimed invention was made. From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious, as evidenced by the references, especially in the absence of evidence to the contrary.

No claim is allowed.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703)308-4227.

An inquiry concerning this communication should be directed to Examiner Suzanne Ziska, Ph.D., at telephone number 703-308-1217.

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SUZANNE E. ZISKA
PRIMARY EXAMINER
GROUP 1800
1/31/94